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| 10/664,358 | 09/20/2003 | Craig A. Rosen | PS905 | 5175 |

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| EXAMINER | |
|---|---|
| ROBINSON, HOPE A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 04/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/664,358 | ROSEN ET AL. | |
| | Examiner | Art Unit | |
| | Hope A. Robinson | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *11-14,17-21,23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,15,16 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Application Status*

1. Applicant's election without traverse of Group I (claims 1-10, 15-16 and 22) on January 27, 2005 is acknowledged. Applicant's comments regarding a rejoinder of method claims upon notification of an allowable product is noted.

2. Claims 1-4, 11 and 22-23 have been amended. Claims 1-24 are pending. Claims 1-10, 15-16 and 22 are under examination. Claims 11-14, 17-21 and 23-24 are withdrawn from further consideration pursuant to 37 CFR 1.12(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

3. The Amendment filed on January 27, 2005 has been received and entered.

### *Specification*

4. The specification is objected to because of the following informalities:

(a) The specification is objected to because trademarks are disclosed throughout the instant specification and not all of them are capitalized or accompanied by the generic terminology. The use of the trademarks such as TAQMAN®, AMPLITAQ GOLD®, for example, have been noted in this application (see page 33). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort

made to prevent their use in any manner, which might adversely affect their validity as trademarks.

(b) The specification is also objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See for example pages 30, 35 and 38. It is suggested that http:// is deleted.

(c) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Polynucleotide Encoding Human Secreted Proteins".

Correction is required.

### *Claim Objection*

5. Claims 1-4 are objected to because of the following informalities:

For clarity and precision of claim language it is suggested that the reference made in the claims to "Table 1A" is deleted from the claims since the specific sequence and notation is recited in the claims.

Correction of the above is required.

### *Information Disclosure Statement*

6. The Information Disclosure Statement filed on January 27, 2005 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

***Claim Rejections-Utility Rejections Under 35 USC § 101 And 35 USC 112, First Paragraph***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-10, 15-16 and 22 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, substantial, specific, or well-established utility. Claims 1-10, 15-16 and 22 are directed to an isolated polynucleotide encoding a polypeptide, vector, host cell, gene corresponding to the polynucleotide and a method of making the polypeptide. The claimed polynucleotides are not supported by either a specific and substantial asserted utility or a well-established utility. The specification fails to provide objective evidence of any activity for the encoded proteins. A well-established utility is a specific, substantial, and credible utility that is well known, immediately apparent or implied by the specification's disclosure of the properties of a material. There is no specific disease or specific function that is suggested for the polynucleotides or the encoded polypeptides. It is noted that page 22 of the specification indicates that the invention relates to human secreted proteins/polypeptides, and isolated nucleic

acid molecules encoding said proteins/polypeptides, useful for detecting, preventing, diagnosing, prognosticating, treating and/or ameliorating cardiovascular diseases, disorders and or conditions related thereto, however, no specific association is made or demonstrated. No real association is made between a specific disorder/disease and the claimed products. A search of the claimed sequences produced a reference that teaches a fragment of the sequence claimed (SEQ ID NO:36) that is 97.5% identical to a sequence disclosed as SEQ ID NO:12026 that comprise unknown single nucleotide polymorphism in known genes (see U.S. Patent No.6,812,339 and the alignment) which does not substantiate the claimed invention.

The specification does not disclose any particular conditions wherein there is a deficiency or overproduction of the claimed polypeptide. What disorder/disease results from a decreased expression or activity of the polypeptide, the specification does not disclose specific information. No evidence is provided, for example, that the encoded polypeptide is not expressed in healthy tissues. It could be a constitutively expressed gene, and thus would not be useful in developing drugs for any disease. Even if it were differentially expressed in disease tissues, for example, there is no indication regarding how to develop a drug to treat specific diseases, because there is no information disclosed regarding the role the polypeptide plays in healthy tissue. For example, page 26 of the instant specification state that cardiovascular diseases and disorders can be treated with the claimed proteins, however, no evidence is provided of the reduction in cardiovascular disease/disorders or the treatment of cardiovascular disease/disorders nor is there any evidence of said protein in association with cardiovascular disease. Thus, no empirical evidence exists on the record to demonstrate the association as claimed between the claimed protein and heart disease or any other diseases. The specification contains several Tables which do not provide any

evidence to demonstrate nor describe the claimed invention. A search of the encoded protein (SEQ ID NO: 549) against the DNA database produced a reference that teaches a DNA encoding a protein, that is 100% identical to the encoded protein (see attached Accession No. AAY87141), said to be useful for hepatic disease, schizophrenia, osteoporosis, AIDS, Alzheimer's disease, to name a few. The reference provides a laundry list of diseases/disorders to which a protein that is structurally identical to the instant encoded protein is suppose to be able to treat. This demonstrates the fact that no specific disease/disorder is associated with the claimed protein. Therefore, the reference does not substantiate the instant disclosure that the encoded protein regarding the claimed protein and cardiovascular disease or any other disease or provide support for a substantial utility.

The specification asserts that the products of the invention can be used (1) as drugs for the treatment or prevention of cardiovascular disease (2) in diagnosing disease and (3) as probes. As for drugs for the treatment or prevention of cardiovascular disease, this asserted utility is not substantial. The specification does not disclose any particular conditions wherein there is a deficiency, overproduction, or altered form of the claimed polypeptides. The fact that the polynucleotide can be found in libraries of cells isolated from for example, disease tissues or immune system cells would not indicate to one of skill in the art that the protein is involved with any of the above conditions. Even if it were differentially expressed in disease tissues, for example, there is no indication regarding how to develop a drug to treat any specific disease based on the protein, because there is no information disclosed regarding the role the protein plays in healthy tissue. Significant further experimentation would be required of the skilled artisan to identify individuals who would benefit from such a drug, and then to determine a best

course of treatment. There is no disclosure, for example, of how to assay for improvement or intolerable levels of side effects or dosages of the drug. Since this asserted utility is not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

It is asserted that the invention can be used in diagnosing disease with the protein, this assertion is not substantial. The specification does not disclose any specific diseases associated with altered levels or forms of the encoded protein as discussed above. Significant further experimentation would be required of one skilled in the art to identify individuals having such a disease. There is no indicia, for example, of any symptoms associated with such a disease/disorder. As this asserted utility is not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. The assertion is made of a use as probes; however, this utility is not specific, as this can be done with any polynucleotide. Expressed polynucleotides have a variety of general uses, for example, as a probe for hybridization or as a template for protein expression, these uses are applicable to any expressed polynucleotide and are not specific to the claimed polynucleotide. MPEP 2107.01 states that, "Utilities that require or constitute carrying out further research to identify or reasonably confirm 'real world' context of use are not substantial utilities".

In view of the foregoing, and absent data/evidence, the claimed invention lack utility. See *Brenner v. Manson*, 383, U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is a reward for the search, but compensation for its successful conclusion". A patent is therefore not a license to experiment. See also the Utility Guidelines available at www.uspto.gov.

8. Claims 8-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 8 is directed to a method with no method steps. As the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. Without setting forth any steps involved in the process/method, results in an improper definition of a process and is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). Note that claims 9-10 are included in this rejection because the claims do not rectify the deficiency in independent claim 8.

9. Claims 1-10, 15-16 and 22 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

In addition the amount of experimentation required to practice the claimed invention is undue as the claims encompass an unspecified amount of fragments that are not supported by the instant specification. The encoded polypeptide as claimed once modified might not have the same properties of the native/wild-type protein or retain the same function. In addition, claims reciting percent sequence identity, for example 95% sequence identity do not indicate where variations will occur or what variations can be tolerated in the sequence. The instant

specification does not demonstrate or provide guidance as to what the structure of the protein will be once modified or if said protein will be functional or exhibit the same properties or characteristics as the native protein. In the instant application, the partial structure in the form of the recited percent identity is insufficient to determine a chemical structure for the variants encompassed in the claims.

Additionally, there is no data provided demonstrative of a particular portion of the structure that must be conserved. Note that the claims do not have a functional limitation, thus, modifications to the polypeptide sequence, may result in a protein that is at best has a different function or at worst has no activity. Due to the large quantity of experimentation necessary to generate the infinite number of variants/fragments recited in the claims and possibly screen same for activity and the lack of guidance/direction provided in the instant specification, this is merely an invitation to the skilled artisan to use the current invention as a starting point for further experimentation.

Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (for example, expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, for example, multiple substitutions. In this case, the necessary guidance has not been provided in the specification. Therefore, while it is known in the art that many amino acid substitutions are possible in any given protein, the positions within the protein's

sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to the protein's structure/function relationship. It is also known in the art that a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. For example, various sites or regions directly involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected (see Wells, Biochemistry, vol. 29, pages 8509-8517, 1990). The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not, and it provides no working examples of any variant sequence that is encompassed by the claims. It is in no way predictable that randomly selected mutations, such as deletions, substitutions, additions, etc., in the disclosed sequences would result in a protein having activity comparable to the one disclosed. As plural substitutions for example are introduced, their interactions with each other and their effects on the structure and function of the protein is unpredictable. The skilled artisan would recognize the high degree of unpredictability that all the fragments/variants encompassed in the claims would retain function. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).*

10. Claims 1-10 and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to an isolated nucleic acid molecule that comprises a first polynucleotide sequence at least 95% identical to a second polynucleotide sequence selected from for example a polynucleotide fragment of SEQ ID NO:36 (see claim 1). The claimed nucleic acid molecule is said to encode a protein (SEQ ID NO:549), however, no function is associated with the protein, thus, the claimed nucleic acid has no ascribed function. The claims are directed to fragments of the claimed nucleic acid and the encoded protein and the claims are absent functional language, therefore, a skilled artisan would not know if said fragments had the same function as the wild-type or a different function. The specification lacks adequate written description to demonstrate to a skilled artisan that applicant was in possession of the claimed invention.

In addition, the claimed invention lacks complete deposit information. The specification on page 40 makes reference to deposits made to ATCC and the claims are directed to ATCC Deposit No. 209224, however, this is insufficient assurance that all of the conditions of 37 CFR 1.801-1.809 have been met, because the specification does not indicate whether the sequence of the invention contained in ATCC Deposit No. 209224 is known and publicly available or can be reproducibly isolated. Without publicly available deposit information one skilled in the art could not be assured of the ability to practice the invention as claimed. It is noted that applicant made

the deposits under the Budapest Treaty, however, the specification need to be amended to disclose the date of the deposit and the public availability of the deposit. For further information concerning deposit practice, applicants attention is directed to *In re Lundark* 773 F 2d 1216 227 USPQ CCAFC and 37 CFR 1.801-1.809.

Moreover, the claims are directed to nucleotide sequences that comprise sequential deletions from the C or N terminus and there is no limit on the amount of nucleotides that can be deleted, and no demonstration of any conserved region or the effects of the modifications contemplated. The claims are also directed to a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides set forth in the claim 1, for example. The claims do not set forth the hybridization conditions that are considered to be stringent and it is known in the art that hybridization conditions can vary. Further, a polynucleotide that hybridizes to the claimed sequence may not have the same function or encode said protein. The claims are also directed to a host cell and methods of making the protein using the recited DNA and as these claims do not rectify the issues raised they also lack adequate written description.

Thus, in view of the foregoing the claimed invention lacks proper written description and the skilled artisan cannot envision the detailed chemical structure of all the claimed fragments encompassed by the claims. Additionally, the instant specification has not provided a representative number of species for the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other

physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. The claimed genus of polypeptides could include non-functional proteins or proteins with a different function than the one described. Therefore, the genus of claimed polypeptides encompasses widely variant species. Based on the unlimited variations contemplated one skilled in the art would at best expect a protein that is different or at worst a protein that is not functional.

*Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991)*, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 1-10 and 15-16 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 1 is indefinite for the recitation of "or a full length polypeptide encoded by the HBIAE26 cDNA Clone ID in ATCC Deposit No:209224 corresponding to SEQ ID NO:549", as this implies that the cDNA sequence is SEQ ID NO:549 which is actually the sequence of the polypeptide. The claim is also indefinite for the recitation of "hybridizing under stringent conditions" as it is unclear what condition applicant is referring to as the art recognizes that hybridization conditions vary. In addition, item (f) of the claim refers to "A residues or T residues" and the art generally recognizes the term "residues" in association with an amino acid sequence and the term "nucleotides" in association with a DNA sequence. Claim 1 is also indefinite for the recitation of "said fragment has biological activity" because it is unclear what function the protein has, note that the instant specification does not disclose a specific function (see item (d)). The dependent claims hereto are also included in this rejection because they do not rectify the deficiency.

Claim 3 is indefinite for the recitation of "is hybridizable to SEQ ID NO:36" because it is unclear what hybridization conditions are desirable whether it is low, moderate or high stringency and what conditions fits each category.

Claim 5 is indefinite for the recitation of "comprises sequential nucleotide deletions" as the entire C or N terminus could be deleted as there is no upper limit.

Claims 15 and 16 are incomplete therefore indefinite because the claims depends from a non-elected claim.

***Conclusion***

12. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner

9/4/05